

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 8 and 12 are cancelled. Claims 15-34 are withdrawn. Claims 1-7, 9-11, and 13-14 are therefore pending in this application. Applicants reserve the right to pursue the subject matter of the cancelled claims in this application or in one or more divisional or continuation applications.

I. The Rejection

The Examiner rejected claims 1-7, 9-11, and 13-14 under 35 U.S.C. 103(a) as being allegedly unpatentable over Wiedmann *et al.* (US Patent No. 5,747,001) (“Wiedmann”) in view of Desai *et al.* (US Patent Publication No. 2007/0117862) (“Desai”). The Examiner acknowledges that “Wiedmann lacks teachings on sterile filtration.” See Office Action, page 3. However, the Examiner cites to Desai as teaching “a process for preparing unusually small nanoparticles of less than 200 nm in diameter, which can be sterile-filtered, through a 0.22 micron filter (see [0051]).” The Examiner concludes that the claims are obvious “because sterilized formulations are safer and beneficial to recipients . . . one of ordinary skill in the art would be motivated to implement the sterile filtration of Desai *et al.* instead of the simple filtration of Wiedmann.” Office Action at page 4.

II. With a Correct Reading, the References Do Not Provide a Finding to Support a Claim for Obviousness

The Examiner clearly identifies her rationale for finding the claims obvious:

“[T]he claims would have been obvious because the technique for improving a particular product was part of the ordinary skill in the art, in view of the teaching of the technique for improvement in other situations.”

Office Action at page 4.

To reject a claim based upon the above rationale, the Examiner must articulate “a finding that one of ordinary skill in the art could have applied the known “improvement”

technique in the same way to the “base” device (method or product) and the results would have been predictable to one of ordinary skill in the art. See Examination Guidelines for Determining Obviousness Under 35 U.S.C. §103, Federal Registrar, Vol. 72, No. 195, pg. 57530, Wednesday, October 10, 2007.

In other words, A) the Examiner must articulate a finding that one of ordinary skill in the art would apply the sterile filtering technique that is applied to the formulations in Desai in the same way to the formulations as taught in Wiedmann, and B) that the results (i.e., a sterile filtered nanoparticulate beclomethasone dispersion with tyloxapol as a surface stabilizer) would have been predictable to one of ordinary skill in the art.

A. Desai Does Not Support a Finding that Sterile Filtration can be Applied to the Formulations in Wiedmann

The reasons that Desai does not support a finding that one of ordinary skill in the art would apply the sterile filtering technique used on the formulations in Desai in the same way to the formulations of Wiedmann are twofold. First, Desai does not teach or fairly suggest that its sterile filtration techniques can be applied to a non-polymeric nanoparticle. Second, Desai differentiates its polymeric nanoparticles from what Desai considers to be “conventional” surface-stabilized nanoparticles, which are taught by Wiedmann.

First, Desai does not teach or fairly suggest that its sterile filtration techniques can be applied to a non-polymeric nanoparticle. Desai describes compositions of nanoparticles comprising pharmacologically active agents and a polymeric core. See Office Action, Abstract, and page 5, paragraph [0045]. Desai admits that he was unsuccessful in formulating nanoparticles of the active agent without using the polymeric core, e.g., by using “conventional surfactants¹” to stabilize the nanoparticles of the active agent. In fact, Desai states: “it is **not possible** to form nanoparticles while using conventional surfactants.” See page 15, Example 2 and Example 3 of Desai. Desai illustrates this phenomenon by demonstrating that when pharmacological agents are mixed with a Tween® surfactant, “large needle-like crystals of the drug” formed with sizes in the range of 0.7-5 microns. See page

¹ “Surface stabilizer” and “surfactant” are understood to be interchangeable in this case.

15, Example 3, of Desai. Desai does teach that nanoparticles with a polymeric core mixed with conventional surfactants did not aggregate. See page 19, Example 18 of Desai.

Desai therefore teaches one of ordinary skill in the art that compositions comprising a polymeric core can be sterile filtered through a 0.2 micron filter, and that compositions comprising a polymeric core *in combination with a surfactant*, can be sterile filtered through a 0.2 micron filter. However, neither of these teachings are germane to whether a non-polymeric nanoparticle (i.e., one with the “conventional” surfactants according to Desai) can be sterile filtered. Thus, Desai does not teach or fairly suggest that its sterile filtration techniques can be applied to a non-polymeric nanoparticle.

Second, Desai differentiates its polymeric nanoparticles from what Desai considers to be “conventional” surface-stabilized nanoparticles of Wiedmann. Wiedmann teaches aerosols containing beclomethasone nanoparticle dispersions. The beclomethasone particles have a surface modifier (i.e., a surfactant) on the particles. The particles of the aerosols of Wiedmann do not utilize a polymeric core, but instead utilize some of the same surface stabilizers that Desai dismisses as non-functional, e.g., Tween® (see col. 3 ln. 40 to col. 4, ln. 67 of Wiedmann). Thus, Desai differentiates its polymeric nanoparticles from what Desai considers to be “conventional” surface-stabilized nanoparticles of Wiedmann. A person of ordinary skill in the art would therefore not be inclined to apply sterilization techniques useful for polymeric nanoparticles of Desai to non-polymeric nanoparticles of Wiedmann.

In conclusion, because Desai does not teach or fairly suggest that its sterile filtration techniques can be applied to a non-polymeric nanoparticle and Desai differentiates its polymeric nanoparticles from the nanoparticles of Wiedmann, Desai does not provide a finding that the “improvement” techniques of Desai can be applied to the “base” product of Wiedmann. Accordingly, the Office Action has failed to provide a finding that one of ordinary skill in the art would apply the sterile filtering technique that is applied to the formulations in Desai et al. in the same way to the formulations as taught in Wiedmann. Without this finding, the Office Action rationale cannot be used to support its conclusion of obviousness. Withdrawal of the rejection is respectfully requested.

B. The Results of Applying the Sterile Filtration Technique in Desai Would Not Have Been Predictable to One of Ordinary Skill in the Art

A second reason that the rejection should be withdrawn is because the Office Action fails to provide a finding that the results of applying the sterile filtration technique of Desai to the formulations of Wiedmann would have been predictable to one of ordinary skill in the art.

First, as acknowledged in the Office Action, "Wiedmann lacks teachings on sterile filtration." Office Action at page 3. No inference or conclusion can properly be drawn therefrom with respect to the predictability of using filtration to sterilize the aerosols of Wiedmann.

Second, as discussed above, Desai applies sterile filtration to nanoparticles having a polymeric core. Desai does not apply sterile filtration to nanoparticles that do not employ a polymeric core. No inference or conclusion can properly be drawn therefrom with respect to the predictability of using filtration to sterilize the particles in the aerosols of Wiedmann because they do not employ a polymeric core.

Finally, the Examiner has not given appropriate weight to Applicants' evidence of the unpredictability of utilizing filtration to sterilize the nanoparticles of beclomethasone or budesonide stabilized with tyloxapol. Applicants have demonstrated and discussed in Examples 5-9 and 12-18 of the instant application, the inability to sterile filter a nanoparticulate budesonide or beclomethasone having a surface stabilizer other than tyloxapol.

Neither Wiedmann nor Desai provide any basis to support the predictability of the application of sterile filtration of Desai to the nanoparticulate beclomethasone of Wiedmann. In fact, Applicants' own application is evidence of the unpredictability of sterile filtration of nanoparticulate beclomethasone and budesonide.

Accordingly, the Office Action has failed to provide a finding that one of ordinary skill in the art would apply the sterile filtering technique that is applied to the formulations in Desai to the formulations in Wiedmann and obtain predictable results. Without this finding,

the Office Action rationale cannot be used to support its conclusion of obviousness.
Withdrawal of the rejection is respectfully requested.

III. Conclusion

Applicants believe that the present application is now in condition for allowance.
Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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